then, the labours of the British Indian Commission go for naught? And are the enormous present sales of this salt compatible with entire lack of "clinical observation"? Other instances of the same determined disbelief are the sweeping and utter condemnation of the use, as such, of cardiac depressants like aconite or American hellebore—the doubt of any efficacy of phosphorus in neuralgia—and the omission of all mention of the antiseptic use of quinia. At the same time, curiously contrasted with this turning of the cold shoulder towards the new, is an occasional clinging to ancient therapeutic notions now commonly thought to be error; as where we are told that perhaps, after all, a probably inert preparation of conium may determine the dissipation of a cancer, or the resolution of a hyperplasia of the liver.

But enough of fault-finding. No one that lives can sit as judge in therapeutics without thereby setting himself up as a mark for some one's poisoned shaft. And so, having sent off the sharpest arrow in our quiver, we will frankly confess that the rest, if shot, would probably be bewitched into boomerangs by the magic of our target, and return to bruise the hand of the sender. Prof. Stillé has worn the ermine in the therapeutic court too long to be lightly impeached, and if exceptions to his decisions be taken, where shall we look for a higher Court of Appeals?

As a whole, the "National Dispensatory" not only makes good its right to exist, but proves itself a work which no progressive physician or pharmacist will dare to be without. It is handsomely gotten up, and is remarkably free from typographical errors.

E. C.

Art. XXII.—*The Croonian Lectures on Certain Points connected with Diabetes.* Delivered at the Royal College of Physicians. By F. W. Pavy, M.D., F.R.S. 8vo. pp. viii., 126. London: J. & A. Churchill, 1878.

The views which Dr. Pavy holds, as expressed in this his latest communication, concerning the physiological relations of the liver to the normal appropriation of sugar, and its share in the production of diabetes, differ so slightly from those with which the profession has so long been familiar, that their statement here, further than is essential to the correct appreciation of the new arguments which he has advanced in their support, may be dispensed with. He maintains that the liver, instead of being a sugar-forming, is essentially a sugar-assimilating organ. In a condition of health, he holds that the amyloid substance of the liver is never converted into sugar; but in deviations from the state of health, sugar, in more or less quantity, does reach the circulation, and, as a consequence, appears in the urine in corresponding quantity; and that when the assimilative action of the liver is properly exerted, so little sugar is allowed to pass into the general circulation, as to be insufficient for rendering the urine more appreciably saccharine than is observed in general health; but when its assimilative function is not properly exerted, ingested sugar is allowed to pass, and in proportion as it does so the urine acquires a more or less saccharine character. It is seen, then, that the constant presence of sugar in normal urine is assumed as an axiom by Dr. Pavy, as a corollary from which follows his doctrine that the difference in elimination of sugar between the diabetic and healthy individual is merely a difference of degree, the sugar in both instances representing the unconsumed residue of ingested sugar, or sugar factors. Although Dr. Pavy lays great stress on the value which this assumption possesses in the support of his views, we cannot, however, see that he has produced any fresh arguments in its support, or has settled the differences between Kühne, Seegen, and others. For while perhaps justly questioning the results obtained by the ordinary application of Trommer's, or the fermentation test, his results of the examination of *three* specimens of healthy (?) urine simply demonstrate the superior delicacy of Brücke's lead process, while no note having been taken of the dietetic condition of the individual, or of the persistence of the sugar, we cannot accept, as demonstrated from so few and imperfect observations, the statement that sugar is invariably a normal constituent of healthy urine.

The vital point of difference between the views of Dr. Pavy and those taught by Bernard, concerning the nature of diabetes and glycogenesis, is that while Bernard maintained the idea of an ingress of sugar, on the one hand, into the general circulation from alimentation and hepatic formation, and its destruction, on the other hand, in the peripheral capillaries, and, the balance being destroyed, that diabetes is due to an increased formation of sugar, Pavy denies all sources of sugar, except that directly ingested, and holds that diabetes is due to a decreased destruction.

In support of these convictions Dr. Pavy here alludes as conclusive, to his earlier observations as to the *post-mortem* production of sugar by the liver; but his experiments are so well known, and his conclusions therefrom so generally mistrusted, from the positive experiments of Flint, Dalton, Lusk, etc., that it is not needful here to discuss them, simply alluding to the fact that the demonstration of a *post-mortem* production of sugar by the liver does not prevent the conception of the *ante-mortem* exertion of that function; and is, in fact, only in accordance with what is observed in other organs—as, for example, the conversion of zymogen into trypsin, and the *post-mortem* development of the amylolytic ferment in a pancreas, from which all that ferment existing at the moment of death had already been extracted; and the statement that the portal blood contains as much sugar as the blood of the hepatic vein, is vitiated by the omission of a ligature to the portal vein before removal of the liver; as otherwise, the portal and hepatic veins, having no valves, the blood is not prevented from regurgitating into the portal (Brunton). It is also worthy of notice that Dr. Pavy still allows the existence of "a trace" of sugar in livers placed in a position to "prevent a *post-mortem* production of sugar."

We cannot therefore admit, with Dr. Pavy, that the glycogenic function of the liver is simply a *post-mortem* process; and even were there stronger arguments in its favour than have yet been adduced, we should hesitate in adopting the conclusion that when a substance like glucose invariably appears in an animal tissue after death, and even in tissues removed before death, with such rapidity that the interval is to be counted by seconds (*three seconds*), that substance was not there before death (Dalton).

We can, however, coincide with Dr. Pavy's criticism of Bernard's latest method of analysis. The point which Dr. Pavy makes, is that in Bernard's process (which depends upon the fact that in an organic fluid containing sugar, the sub-oxide of copper can be prevented from precipitation by the employment of a sufficient quantity of concentrated potash solution, the effect being a simple decoloration of the fluid); "the potash and the organic matter lead to the development of a reducing substance, which, without the presence of sugar, produces a decoloration of the test." In other words, he claims that Bernard's quantitative analyses of fluids supposed to contain sugar have really been analyses of fluids which contain no sugar at all, and have been estimations of some third quantity; an assertion which seems to be substantiated by Dr. Pavy's experiment, in which, in a fluid prepared from dog's blood in which the trace of sugar that was originally present had been destroyed by boiling with causticpotash, and which subsequently gave no reaction with Trommer's test, when treated by Bernard's process gave the result which Bernard had stated to be characteristic of the presence of sugar. Pavy explains this result as due, not directly to the organic matter to which the suspension of the sub-oxide has been attributed, but to the ammonia of which it is a source, while the reduction of the copper is due to some unknown factor.

Bernard's later analyses of the amount of sugar in the liver at the moment of death, are also discussed, and here again, with great justness, he takes exception to Bernard's process, claiming that the insertion of 20 gms. of liver into only 60 gms. of boiling water, cannot immediately coagulate all the sugar-producing ferment which is known to exist in the liver, or in the blood as others would have it. The effect must be to temporarily reduce the temperature of the water, and so favour the condition which the experiment is designed to prevent. It is to be remarked, however, that even by Pavy's accepted method he still obtains a trace of sugar.

In studying the normal amount of sugar in healthy blood, Dr. Pavy employs his own gravimetric method of estimating the quantities of sugar, by weighing the amount of reduced copper deposited by galvanic action on a platinum cylinder. He prefers to collect the blood at the moment of death of the animal, but before it can be influenced by the *post-mortem* action of the liver, as then, the perturbing influences necessary in the operation are avoided. Consequently, if Dr. Dalton's results are due to *post-mortem* action of the liver, the blood must be collected and examined in less than three seconds. His examinations of blood conducted in this manner, revealed the presence of sugar in the proportion of from 0.787 to 0.521 per 1000 parts, in opposition to from 1 to 3 parts per 1000, as stated by Bernard; while his examination of the liver when *post-mortem* change is prevented, revealed from 0.056 to 0.597 parts per 1000, in opposition to 1 to 3 parts per 1000, as claimed by Bernard.

Deferring for a moment any comment on these results, let us examine his observation as to the destruction of sugar in the circulation.

To answer the theory of its destruction in the systemic capillaries, comparative analyses are made of the venous and arterial blood, and he states that even if there should be found more sugar in the arteries than in the veins, there need not necessarily be invoked the *destruction* in the capillaries, as the loss may have been due to mere osmosis. He also directs attention to the fallacy apt to complicate results, in which the blood was not drawn simultaneously from artery and vein, and thinks this may explain the discrepancy between his results and Bernard's. Though it seems that his method of first killing the animal, and then "drawing a scalpel across the artery and vein determined upon, without any attempt at isolation," leaves a great deal to be desired as regards precision and reliability as to the exclusive source of the blood, and that, too, in experiments which are expected to show how errors from carelessness are to be avoided. Even in these we notice a slightly higher average in favour of arterial blood—arterial .8475, venous .8347, leaving an excess for arterial blood of .013—while his experiments relating to blood drawn in life show 0.003; results which he states are so small, the excess being first on one side and then on the other, as to permit of their being attributed to deficiencies of the method.

When we notice, however, that no note is made of the nutritive condition of the animals experimented upon, the amount of glycogen in the liver or in the muscles, and when we remember that the muscles have the power of taking up sugar from the blood, and converting it into glycogen (Weiss), of forming sugar again from this glycogen, and of changing both the sugar they form and the greater part of that which they receive from the blood into lactic acid and glycerine which undergo combustion, and when we remember that Ludwig and Genersich have *demonstrated* a reduction of sugar in blood which passes through *contracting* muscles, the observations of Dr. Pavy are not of much importance, particularly as in experiments the muscles were at rest, and it is known that muscles at rest receive comparatively little arterial blood. And then clinically it has been shown that muscular exertion will diminish the amount of sugar excreted in diabetes. (Senator.)

His conclusions, however, are that there is only a small amount of sugar in the blood, there is constantly a small amount in the urine, and any difference between the amount of sugar in arterial and venous blood is too small to be considered of any significance.

In fact, he says that no evidence of destruction of sugar in the economy has been furnished, and he holds that "corresponding with the amount of sugar in the circulation there is elimination with the urine, and therefore whatever accumulation occurs becomes revealed by the condition of urine;" and he attaches great significance to the fact that, even with the slight amount of sugar found in the blood, there is a constant escape by the urine. That the quantity of sugar in urine is an indication of the condition of the blood is further supported by a table in which their relative proportions are shown, but certainly some explanation should be given of the fact that, although he has claimed that the blood in all localities presents an equal proportion of sugar, the proportion of sugar in the urine should be more than twenty times greater than that of the blood. If this relation is as fixed and definite as Dr. Pavy claims, we would expect that the condition of the blood would also indicate the condition of the urine, as he has expressly declared "that, corresponding with the amount of sugar existing in the circulation, there is elimination with the urine;" and we would, therefore, expect that in those animals whose blood was shown to contain about 0·5 parts per 1000, their urine should have contained 10.0 parts per 1000. We doubt, however, if such was the case; and if we are mistaken then the animals were diabetic, and should not have been used in conducting investigations as to physiological conditions. The observation as to diffusion of sugar has here, of course, no force, and in fact was created to explain the fact that sugar may be introduced into the circulation without appearing in the urine.

As regards the materials which go to form glycogen, Dr. Pavy is in accord with most observers, and we also notice that he states when "sugar is voided upon a strictly animal diet, . . . such sugar may be put down as taking origin from the abnormal descent of the amyloid substance derived from nitrogenous matter." He, however, persistently declares, from the considerations above alluded to, that it never, except under unnatural condition, passes into sugar, but, he thinks, gives origin to fat, although the only evidence that can be adduced as to such transformation is that the carbo-hydrates, from most of which glycogen can be produced, lead in some way or other to the accumulation of fat in the body, "but no one has yet been able even to suggest the way in which glycogen could be converted into fat." (Foster.)

These, then, are his opinions as to the physiological relations of sugar to the organism, and he next takes up its pathological relations in the production of diabetes.

Believing it demonstrated that the quantity of sugar in the urine is directly dependent upon the quantity of sugar circulating in the blood in both health and disease (this normal minute quantity being derived from that absorbed by the thoracic duct), and that normally all the sugar and glycogen factors injected in the food become converted in the liver into amyloid substance, which in its turn never *normally* becomes sugar, but is destined to form fat, he holds that diabetes must be due to some condition which mainly prevents the conversion of sugar into amyloid substance, and secondarily favours the transformation of the latter into sugar, although he subsequently states that he inclines to the opinion that diabetes results simply "from the simple passage of sugar through the liver." A theory, however, which is rendered untenable by the fact that Grobe has found glycogen, though in small quantities, in the liver of a diabetic; and it has been found that the excretion of sugar can be increased by the administration of glycerine, a substance which forms sugar only after having been converted into glycogen in the liver. So, too, when the sugar puncture is performed in an animal in which the formation of glycogen has been prevented by arsenic, glycosuria is not produced.

The production of diabetes, however, he believes to be dependent upon an excess of arterial blood in the portal circulation, and details in its support an experiment in which the injection of defibrinated arterial blood into the portal vein was followed by marked glycosuria, while a similar procedure with venous blood had no effect. Although this explanation seems to account satisfactorily for the production of diabetes from nervous lesions, that is, as far as the undoubted concurrence of diabetes and disturbance of the abdominal circulation, in support of which he makes the extravagant statement that the redness of the tongue in diabetes may be considered as an index of the over-arterialized condition of the portal blood, it hardly seems that such a marked perversion of glandular action could follow a mere increase in its supply of oxygenated blood—that we could have an entire suspension of its normal function and its direct contrary established. We might imagine, as would accord with the theory of glycogenesis, that an increased arterial supply might cause an increased functional activity, but hardly the conditions accepted by Dr. Pavy. But, besides, Dr. Pavy has himself brought forward facts which increase the difficulty attending the acceptance of his views, such as the ligature of the vena porta, by which, of course, an excess of arterial blood was not created, and yet there was an increase of sugar in the blood with an ingenious explanation as to why it did not appear in the urine; and then, if we are to infer from the context that in this condition the liver received arterial blood alone (hepatic artery), and hence diabetes, we would expect that section of the vaso-motor nerve accompanying these vessels, by which the arterial blood-supply would be increased, would be followed by diabetes. Dr. Pavy's earlier observations, however, have proved this not to be the case.

But then Dr. Pavy has also shown that an excess of venous blood in the liver, as in asphyxia, may be productive of diabetes. This condition of affairs, which he believes is only *apparently* inconsistent with his views as to the arterial production of diabetes, is explained by the increased pressure to which the hepatic cells are subjected by the venous engorgement causing "more or less transudation and direct admixture of their contents with the blood," and the production of diabetes in a manner analogous to that caused by the direct injection of glycogen into a *vein*. If this is the correct explanation, why does not the injection of venous blood into the portal vein, by which a local venous plethora is produced, cause diabetes?

The production of glycosuria by carbonic oxide is explained by the similarity of action on the hemoglobin possessed by this gas and oxygen.

Going back now to the physiological condition, he states that the reason the glycogen accumulates in the liver is on account of its peculiar venous supply, and offers this condition as an explanation of the development of sugar and absence of glycogen in the early months of fœtal life, when the arterial supply to the liver is very great, and the venous supply comparatively insignificant, while in later months the portal circulation acquires more importance, and hence the conversion of glycogen into sugar is stopped, and glycogen is then to be found in the liver. He also states that the conditions in which glycogen accumulates in other localities is in favour of his view, as in muscles at rest, in hybernation, and in solidified lungs in pneumonia. In other words, glycogen tends to accumulate in certain structures under the existence of a limited supply of oxygen; when more oxygen is supplied it is converted into sugar. It does not seem, however, that this explanation is any more satisfactory than that of Brunton, who attributes the storing of glycogen in such localities to the rapid cell growth there taking place.

Finally, we must take exception as to the manner proposed by Dr. Pavy in which lesions of the nervous system produce diabetes, viz., by causing "the presence of oxygenated blood in the portal vein." For it has been pointed out by many observers, more especially Cyon, that after such lesion it is the circulation in the hepatic artery that is modified while the portal circulation is apparently not affected, while vaso-motor paralysis of the intestine, which he considers "constitutes the key to the explanation of the saccharine condition of the urine in diabetes" when artificially produced, as by section of the splanchnic nerves, not only does not cause diabetes, but even prevents its production by the sugar puncture; the explanation of this fact by Cyon not being adequate to account for its production under Pavy's theory. Besides, it should not be forgotten that the vascular dilatation might be quite a secondary and non-essential phenomenon, as in following out the simile drawn by Dr. Pavy in the case of the salivary glands, the secretion of saliva following stimulation of the chorda is not necessarily due to the consequent vascular paralysis, as the vascular dilatation may be produced, as in atropia poisoning, by stimulation of the chorda without any secretion; and on the other hand secretion may be produced by the same stimulation, even in the absence of the circulation.

In conclusion, we can see no grounds in the arguments here adduced by Dr. Pavy for discarding the opinion that the glycogen of the liver is a reserve fund of carbo-hydrate material to be converted into sugar as the needs of the system require. While diabetes from the passage of ingested sugar unchanged through the liver, if it occur at all, is only one of many ways in which the disease may be produced (see the admirable lectures of Lauder Brunton on Pathology of Diabetes, in *Brit. Med. Journ.* 1874), we cannot consider that Dr. Pavy has proved that the normal function of glycogenesis is due to the presence of venous blood in the portal vein, and the morbid condition of diabetes is due to superoxygenated portal blood.

R. M. S.

ART. XXIII.—*Lectures on Dermatology; delivered in the Royal College of Surgeons of England in* 1876–1877–1878. *Including Derangements of the Colour of the Skin; together with Affections of the Nails, Hair System, and Cutaneous Gland System.* By ERASMUS WILSON, F.R.S., etc. 8vo. pp. 286. London: J. & A. Churchill, 1878.

THE present volume concludes the nine courses of lectures delivered by Mr. Wilson on the foundation established by himself in 1869. It is possible also that it marks the conclusion of dermatological teaching from that chair, since we learn that the scope of the endowment is to be enlarged "to embrace original work in every department of surgical pathology." There is, therefore, a certain, almost pathetic, interest in these lectures, since not only is it unlikely that Mr. Wilson will hereafter publish any other work, but the lectures themselves, now concluded,